REMARKS

1. Preliminary Remarks

a. Status of the Claims

Claims 31, 32, and 39-42 are pending in this application. Claims 32 and 41 are amended. Applicant respectfully requests that the amendments and remarks made herein be entered into the file history of the application. Upon entry of the amendments, claims 31, 32, and 39-42 will be pending and under active consideration.

b. Interview Summary

Applicant would like to thank Examiner McGarry for the courtesy of participating in the interview with Teddy C. Scott on September 13, 2010 (the "Interview"), during which a number of issues were discussed. In particular, the Examiner noted that SEQ ID NO: 6527 recited in claim 31 is longer than the maximum length of the probe described in claim 41, and thus that claim 41 may be indefinite. This supplemental amendment includes an amendment to claim 41 to clarify this issue.

The Examiner also raised the possibility that claim 42 may be indefinite, because this claim relates to a probe of 18-24 nucleotides comprising a nucleic acid of claim 32, while SEQ ID NO: 15 recited in claim 32 is 22 nucleotides in length. To clarify this issue, Applicant is submitting this supplemental amendment to amend claim 32 to include miRNAs of 18-24 nucleotides in length, which are all produced from the same hairpin having SEQ ID NO: 6527.

c. Claim Amendments

(1) Claim 32

Claim 32 is amended to clarify the scope of claim 42, which depends from claim 32. Claim 42 relates to a probe that is 18-24 or 50-120 nucleotides in length, and comprises a nucleic acid of claim 32. Claim 32 relates to a miRNA having SEQ ID NO: 15, which is 22 nucleotides in length. During the Interview, the Examiner raised the possibility that claim 42 may therefore be indefinite. At the time of filing, however, one of ordinary skill in the art recognized that miRNAs produced by a particular hairpin were not uniform in length. In fact, miRNAs produced by a hairpin were generally known to vary in length.

This variability stems from an understanding at the time of filing that a protein complex that includes an enzyme called Dicer processes hairpin precursor RNAs into shorter miRNAs of

approximately 22 nucleotides in length.[1] The length of a given miRNA was known to be approximate, because one of ordinary skill in the art knew that Dicer processing does not yield an oligonucleotide that has a fixed length from a given precursor, but rather that Dicer produces oligonucleotides that vary in length between 18-24 nucleotides.[2] Many cloned miRNAs were known to exhibit this kind of length variation at the 3' end.[3] For example, Lim discloses miRNA length ranges of 21-24 (miR-228), 19-23 (miR-233), and 21-25 nucleotides (miR-236), and describes that the length heterogeneity occurs at the 3' terminus.

This knowledge in the art is reflected in the specification of earlier-filed U.S. Patent Application No. 10/707,147, to which this application claims priority (the "Priority Application"). The Priority Application describes how the Dicer enzyme complex processes a hairpin into a miRNA of ~22 nucleotides in length.[4] The Priority Application also more specifically discloses that, "… RNA encoded by the bioinformatically detectable novel gene [i.e., a hairpin-encoding gene] is about 18 to about 24 nucleotides in length, and originates from an RNA precursor [i.e., a hairpin]."[5] Accordingly, the explicit description of a particular miRNA sequence that is 22 nucleotides in length and is produced from a particular hairpin, **necessarily** establishes possession of Dicer-processed 18-24 nucleotide-long variants that are truncated or elongated at the 3' end and are produced from the same hairpin.

Thus, in order to clarify the subject matter of claim 42, Applicant is amending claim 32 to describe the other miRNAs that relate to SEQ ID NO: 15 and are produced from the same hairpin

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[1] *See* Bartel, D.P., "MicroRNAs: Genomics, Biogenesis, Mechanism, and Function," Cell, 2004;116:281-97 at 285, column 2, paragraph 2 ("…Dicer performs an activity in metazoan miRNA maturation similar to that which it performs in chopping up double-stranded RNA during RNAi…").

[2] *See* Zamore, P.D., *et al.*, "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell, 2000;101:25-33 at Figure 3 (showing a gel of oligonucleotides produced by Dicer processing of a precursor, where the gel clearly shows oligonucleotide products of 21, 22, and 23 nucleotides in length) *and see* Elbashir, S.M. *et al.*, "RNA interference is mediated by 21- and 22-nucleotide RNAs", Genes and Development, 2001;15:188-200 at page 190, column 2, paragraph 4 (describing how a dsRNA precursors yielded dsRNA products that **varied in length from 18 to 24 nucleotides**).

[3] *See* Lim, L.P. *et al.*, "The microRNAs of *Caenorhabditis elegans*," Genes & Dev., 2003;17:991-1008 ("Lim" hereafter) at Table 2 *and see also* Morin, R.D. *et al.*, "Application of massively parallel sequencing to microRNA profiling and discovery of human embryonic stem cells," Genome Res., 2008;18:610-21 at Figure 2 and Supplemental Table 4 (showing a number of miRNA that have a length range of at least 20-24 nucleotides, where the length variation occurs at the 3' end).

[4] *See* Priority Application at paragraph 0094 ("An enzyme complex designated DICER COMPLEX, 'dices' the GAM FOLDER PRECURSOR RNA [i.e., hairpin] into GAM RNA [i.e., miRNA], a single stranded ~22 nt long RNA segment. As is known in the art, 'dicing' of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins").

[5] Priority Application at paragraph 0015.

precursor. Specifically, amended claim 32 now recites the related miRNA products of 18-24 nucleotides in length derived from SEQ ID NO: 6527, including the 22 nucleotide-long SEQ ID NO: 15. Accordingly, the amendment to claim 32 obviates any possibility of indefiniteness.

(2) Claim 41

Claim 41 is amended so that the length of the probe is 131 nucleotides in length. This length is identical to the length of SEQ ID NO: 6527, which is contained in the probe. Applicant submits that this amendment obviates any possibility of indefiniteness.

2. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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